

PCT/IL2004/000571

27 JUN 2004

REC'D 15 JUL 2004

WIPO PCT

PA 1179454

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

June 07, 2004

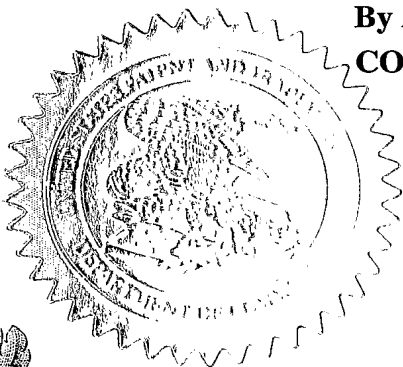
THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE UNDER 35 USC 111.

APPLICATION NUMBER: 60/517,073

FILING DATE: November 05, 2003

PRIORITY DOCUMENT
SUBMITTED OR TRANSMITTED IN
COMPLIANCE WITH
RULE 17.1(a) OR (b)

By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS




M. K. HAWKINS
Certifying Officer

PATENT APPLICATION SERIAL NO. _____

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

11/06/2003 HVUONG1 00000122 60517073

01 FC:2005

80.00 QP

PTO-1556
(5/87)

*U.S. Government Printing Office: 2002 — 469-267/69033

PROVISIONAL APPLICATION FOR PATENT COVER SHEET
This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

INVENTOR(S)					
Given Name (first and middle (if any))	Family Name or Surname		Residence (City and either State or Foreign Country)		
MORDECHAI	DEUTSCH		MOSHAV OLESH, ISRAEL		
Additional Inventors are being named on the _____ separately numbered sheets attached hereto					
TITLE OF THE INVENTION (500 characters max)					
A MICROSAMPLE CELL EXTRACTION TOUCHING METHOD					
Direct all correspondence to: CORRESPONDENCE ADDRESS					
<input type="checkbox"/> Customer Number: _____					
OR					
<input checked="" type="checkbox"/> Firm or Individual Name	SCHOTTENSTEIN CELLOME RESEARCH CENTER				
Address	BAR ILAN UNIVERSITY				
Address					
City	RAMAT GAN	State		Zip	52900
Country	ISRAEL	Telephone	5342675	Fax	+97235342019
ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/> Specification Number of Pages 5		<input type="checkbox"/> CD(s), Number _____			
<input checked="" type="checkbox"/> Drawing(s) Number of Sheets 2		<input type="checkbox"/> Other (specify) _____			
<input type="checkbox"/> Application Date Sheet. See 37 CFR 1.78					
METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT					
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27.				FILING FEE Amount (\$)	
<input checked="" type="checkbox"/> A check or money order is enclosed to cover the filing fees.				80	
<input type="checkbox"/> The Director is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: _____					
<input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.					
The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.					
<input type="checkbox"/> No.					
<input checked="" type="checkbox"/> Yes, the name of the U.S. Government agency and the Government contract number are: <u>US ARMY MEDICAL RESEARCH ACQUISITION ACTIVITY AWARD# DAMD 17-01-1-0131</u>					

(Page 1 of 2)

Respectfully submitted

SIGNATURE

TYPED or PRINTED NAME MORDECHAI DEUTSCH

TELEPHONE +97235344675

Date 11-05-2003

REGISTRATION NO.

(if appropriate)

Docket Number: 27

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop Provisional Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

13281

U.S. PTO

Approved for use through 07/31/2006, OMB 0651-0032
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PTO/SB/17 (10-03)

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27TOTAL AMOUNT OF PAYMENT (\$)
80

Complete if Known

Application Number
Filing Date 11/05/2003
First Named Inventor MOPDECHA DEUTSCH
Examiner Name
Art Unit
Attorney Docket No. 27

METHOD OF PAYMENT (check all that apply)

☒ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None☐ Deposit Account:Deposit
Account
Number
Deposit
Account
Name

The Director is authorized to: (check all that apply)

☐ Charge fee(s) indicated below ☐ Credit any overpayments☐ Charge any additional fee(s) or any underpayment of fee(s)☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1001 770	2001 385	Utility filing fee	
1002 340	2002 170	Design filing fee	
1003 530	2003 265	Plant filing fee	
1004 770	2004 385	Reissue filing fee	
1005 160	2005 80	Provisional filing fee	80

SUBTOTAL (1) (\$)
80

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

Total Claims	Extra Claims	Fee from below	Fee Paid
Independent Claims	-20** =	X	
Multiple Dependent Claims	-3** =	X	

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description
1202 18	2202 9	Claims in excess of 20
1201 86	2201 43	Independent claims in excess of 3
1203 290	2203 145	Multiple dependent claim, if not paid
1204 89	2204 43	** Reissue independent claims over original patent
1205 18	2205 9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) (\$)

**or number previously paid, if greater. For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1051 130	2051 65	Surcharge - late filing fee or oath	
1052 50	2052 25	Surcharge - late provisional filing fee or cover sheet	
1053 130	1053 130	Non-English specification	
1812 2,520	1812 2,520	For filing a request for ex parte reexamination	
1804 920*	1804 920*	Requesting publication of SIR prior to Examiner action	
1805 1,840*	1805 1,840*	Requesting publication of SIR after Examiner action	
1251 110	2251 55	Extension for reply within first month	
1252 420	2252 210	Extension for reply within second month	
1253 950	2253 475	Extension for reply within third month	
1254 1,480	2254 740	Extension for reply within fourth month	
1255 2,010	2255 1,005	Extension for reply within fifth month	
1401 330	2401 165	Notice of Appeal	
1402 330	2402 165	Filing a brief in support of an appeal	
1403 290	2403 145	Request for oral hearing	
1451 1,510	1451 1,510	Petition to Institute a public use proceeding	
1452 110	2452 55	Petition to revive - unavoidable	
1453 1,330	2453 665	Petition to revive - unintentional	
1501 1,330	2501 665	Utility issue fee (or reissue)	
1502 480	2502 240	Design issue fee	
1503 640	2503 320	Plant issue fee	
1460 130	1460 130	Petitions to the Commissioner	
1807 50	1807 50	Processing fee under 37 CFR 1.17(g)	
1806 180	1806 180	Submission of Information Disclosure Stmt	
8021 40	8021 40	Recording each patent assignment per property (times number of properties)	
1809 770	2809 385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810 770	2810 385	For each additional invention to be examined (37 CFR 1.129(b))	
1801 770	2801 385	Request for Continued Examination (RCE)	
1802 900	1802 900	Request for expedited examination of a design application	

Other fee (specify)

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$)

SUBMITTED BY

Name (Print/Type)

DR. Robert VASL

Registration No.

(Attorney/Agent)

(Complete if applicable)

Telephone

+97235344675

Signature

KVASL

Date

11/5/03

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PROVISIONAL PATENT APPLICATION

Inventors: MORDECHAI DEUTSCH

Title: A MICROSAMPLE CELL EXTRACTION TOUCHING METHOD

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to cellomics and, more particularly, to a method employing a collection system for live cells from a tissue with a minimal amount of damage to the tissue.

Tissue specimens for pathological analysis are obtained for histological and pathological observation in order to determine factors such as the characteristic features of the tissue. For the purpose of diagnosis it may be highly advantageous to carry out functional assays on living cells that should be obtained before fixation. This functional assay can only be performed if the cellular extraction will cause minimal damage to the tissue structure under study.

A ubiquitous method used by pathologists employs fixation of thin cuts of tissue with the use of formalin for example. However as stated above, this fixation procedure kills the cells being studied and thus render them useless for functional analysis.

All tissues are open to circulating fluxes of various cells of the immune system. The level and components of this circulation is specifically sensitive to various pathological situations. Functional studies therefore may be instrumental for diagnostic purposes and therefore there is a growing need to extract such cells with a minimal damage to the tissue before regular pathological procedures.

BRIEF DESCRIPTION OF THE DRAWING

The invention is herein described, by way of example only, with reference to the accompanying drawing. With specific reference now to the drawing in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

Figure 1

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

Cells may be observed and/or manipulated in numerous settings known in the art. One example of such a setting is a cell chip (ITICBP assembly) as described by Deutsch in PCT patent application number WO 03/035824 filed 25 October 2001 which enables the observation and manipulation of single cells or a defined amount of cells in their own individual locations.

In the closed ITICBP assembly described in the previous report, only cells in suspension can be loaded. In order to allow loading by 'touch', a direct attachment between the tissue and the ITICBP surface may be performed, while the latter is situated in the cellchip housing/holder. In order to enable a 'touch', a removeable ITICBP sealing cover glass is included in the ITICBP which does not exist in the

former ITICBP as described by Deutsch in PCT patent application number WO 03/035824.

The ITICBP is situated and held in a rubber socket. External pressure exerted on a cover glass on top of the socket, creates a sealed measurement micro liter volume compartment. The rubber socket contains micro channels/pipes, which permit the transfer of cell suspension, in addition to solutions to the cells held in the cellchip.

At this stage, the system channels may be tested by the injection of solution via the micro channels by using needles for example. According to preferred embodiments of the invention a cell chip is made with a removable glass or plastic top. Preferably when the cover is on, the system may be tested for any leaks by flushing the system with a solution. The cover may then be removed and then in order to ensure that there is no air in the system more solution may be added to the system or the solution may be moved backward to the direction that it was introduced as described above such that a droplet may be formed on top of the grid and visible as is seen in figure 1. Now it is ready for touch. The tissue to be studied is laid (touched) on top of the open grid for a short period of time of up to a number of minutes. During this period cells which have been freed by the fresh cutting of the tissue may settle down onto the grid. This freeing of cells and their settling down into the wells may be facilitated by gently splashing the tissue surface adjacent to the wells with solution which may be injected/pumped via the inlet syringe. The tissue is then gently removed from the chip and then the cover glass may then be returned and closed preferably hermetically while preferably refraining from bubble creation.

The cell-laden system may now be exposed to reagents and other fluorescent probes for manipulations and observation.

A typical cell-chip in which each well may be hexagonally shaped will be described here as an example of a cell-chip. This is a dense configuration of wells. Wells that may be fashioned from a rigid source such as glass or a plastic may be surrounded by very sharp tips as shown in figure 2. In performing that procedure, the loaded cells may become damaged (injured) due to the very sharp tips of the 6 columns surrounding each well.

According to further embodiments of the present invention, the problem of cell damage due to sharp tips surrounding the wells may be solved by dulling the well

tips, as can be seen in Fig. 3. Another solution to this problem would be to fashion the wells from a compliant material such as a gel.

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the present specification.

WHAT IS CLAIMED:

1. A method and a system for delivering live cells from a tissue to a cell-chip essentially as described hereinabove or depicted in the figures.

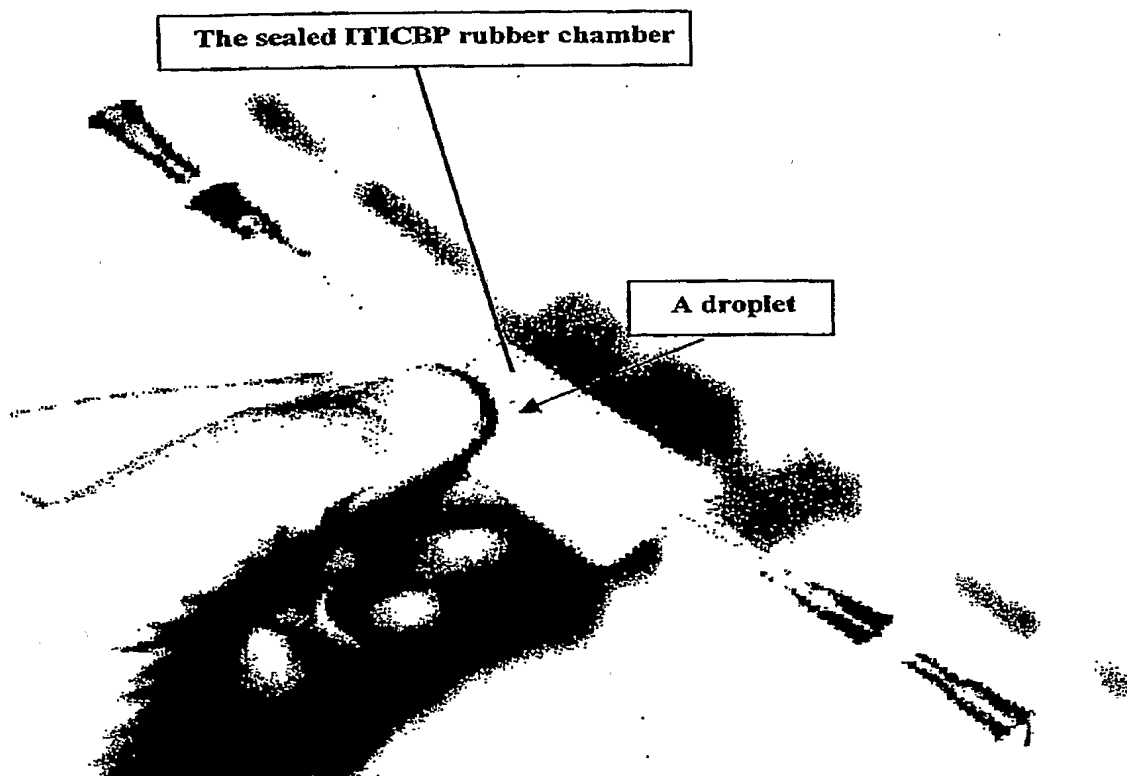
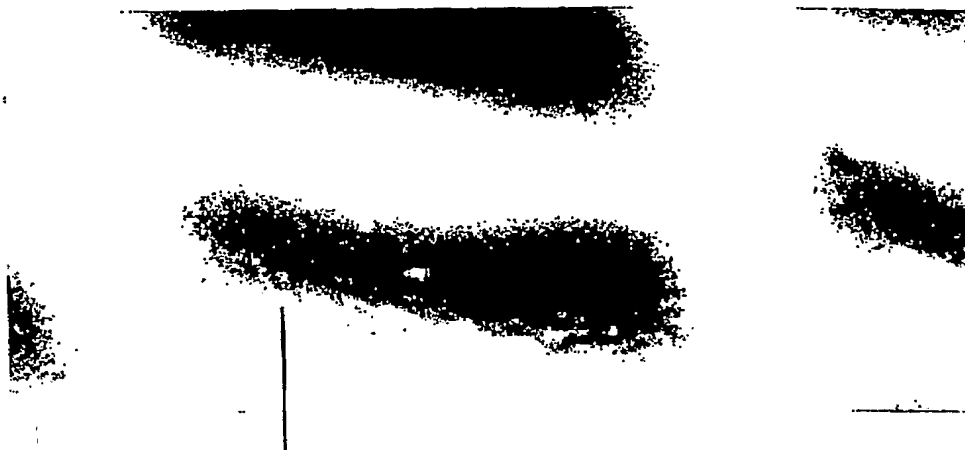


Figure 1



sharp tips

Figure 2



dull tips

Figure 3